

EDITORIAL

Magnetic resonance myocardial perfusion imaging: a new era in the detection of reversible myocardial ischaemia

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In due course, magnetic resonance myocardial perfusion imaging will probably replace SPECT as the most widely used non-invasive method for detecting reversible myocardial ischaemia

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The currently used tests for the detection of reversible myocardial ischaemia have several limitations. Exercise electrocardiography has only moderate sensitivity and specificity (68% and 77%).¹ Single photon emission computed tomography (SPECT) has an improved sensitivity of 86% and an equivalent specificity of 74%, but the radiation exposure is considerable at between 8 and 20 millisieverts depending on the radioisotope used, and the images are often degraded by photon scatter and attenuation artefacts.² Positron emission tomography is widely regarded as the non-invasive gold standard, but it is expensive, requires radioisotopes and has limited availability in the UK. Stress echocardiography does not involve radiation and can be used in conjunction with either exercise or pharmacological stress. It has a sensitivity and a specificity comparable to SPECT, but a proportion of patients have inadequate imaging windows.³ Multidetector computed tomography coronary angiography is a relatively new imaging modality, which was reviewed in *Heart* recently.⁴ As with nuclear imaging techniques, radiation exposure is not insignificant and, similar to conventional coronary angiography, it is not possible to confirm the functional relevance of any stenoses identified by this method.^{5,6}

Magnetic resonance myocardial perfusion imaging (MRMPI) has multiple potential advantages over all of the above techniques. It provides superior spatial resolution, allowing the delineation of both subendocardial and transmural perfusion defects. Most of the currently used perfusion sequences provide a spatial resolution of 2–3 mm² without any orientation constraints or problems with inadequate imaging windows. The currently used perfusion sequences also provide excellent temporal resolution, and 3–4 slices can usually be obtained per heartbeat at the heart rates achieved during pharmacological stress. During stress imaging, the three slices are obtained in the short axis to cover the basal, mid and apical segments of the left ventricle. This protocol covers 16 of the 17 segments of the AHA coronary arterial territory model.⁷

pharmacological stressor and the other for the contrast medium. Gadolinium is the most widely used contrast medium for MRMPI. It shortens the T1 relaxation time of the myocardium, leading to increased signal intensity as it perfuses through the heart. ECG monitoring is essential for scanner triggering and to monitor for arrhythmias. Non-invasive blood pressure monitoring is also mandatory. A specialised receiver coil with multiple coil elements is placed on the patient's chest to achieve the best signal-to-noise ratio (SNR).⁸ After the patient is placed into the magnet, the operator localises images in the axial, coronal and sagittal planes and these are used to obtain the true horizontal long and short axes of the left ventricle. Imaging sequences for the evaluation of myocardial perfusion have evolved rapidly. The initial protocols used single-shot turbo-gradient echo sequences, but now faster sequences using echoplanar imaging are being used more commonly. In addition, parallel imaging techniques such as temporal sensitivity encoding have been introduced to increase spatial coverage without reducing image quality.⁹

Adenosine is the most commonly used agent for pharmacological stress. It produces maximal coronary vasodilatation, and areas of hypoperfusion can be identified by creating a mismatch in coronary flow. Intravenous adenosine is infused at a dose of 140 µg/kg/min for 2–3 min before the injection of gadolinium. The adenosine continues to run for the duration of the gadolinium injection and until the first-pass images are completed. The dose of gadolinium varies in published studies from 0.025 to 0.15 mmol/kg. A higher dose of gadolinium can help in the visual identification of perfusion defects and was considered superior to a lower dose in a multicentre European dose-ranging study.¹⁰ As the gadolinium perfuses, the myocardial areas of hypoperfusion are seen as dark areas of reduced signal intensity (fig 1). At 20 min after the acquisition of the stress images, the perfusion sequence is repeated at rest with the same dose of gadolinium. A reduction in the extent of the perfusion abnormality or complete normalisation of flow in the resting images confirms the presence of reversible ischaemia.

For 24–48 h before adenosine stress, patients with MRMPI should ideally abstain from all methyl xanthine-containing substances such as caffeinated drinks and also theobromines, which

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PROTOCOLS

Before imaging, an intravenous cannula has to be placed in each arm of the patient, one for the

Abbreviations: MRI, magnetic resonance imaging; MRMPI, magnetic resonance myocardial perfusion imaging; SPECT, single photon emission computed tomography

are mainly encountered in chocolate, and theophylline products. These are competitive antagonists of adenosine and may limit the ability to achieve maximal hyperaemia during the adenosine infusion. Adenosine has the advantage of a short half life of <10 s, allowing rapid clearance after termination of the infusion should side effects be encountered. The most commonly reported symptoms are chest tightness, breathlessness, flushing, headache, abdominal pain and dizziness. Atrioventricular block at rest is a contraindication to the use of adenosine, but is rarely encountered during the infusion in patients with normal resting conduction. Adenosine is also contraindicated in patients with reversible airways obstruction as it may provoke bronchospasm. Cine stress imaging during a dobutamine infusion can also be used for the diagnosis of myocardial ischaemia by comparing wall motion and myocardial thickening with resting images. Dobutamine is not as safe an agent as adenosine. However, it has been shown to be superior to adenosine when using new regional wall motion abnormalities as a marker of reversible ischaemia in patients with significant coronary heart disease.¹¹

DIAGNOSTIC ACCURACY

Several recent studies have assessed the sensitivity and specificity of MRMPI for the detection of functionally significant coronary heart disease. Table 1 summarises the findings of some of the larger studies. Most of these studies compared MRMPI with quantitative coronary angiography. However, it is now widely accepted that quantitative coronary angiography does not reliably predict the functional significance of a coronary arterial stenosis.⁵⁻⁶ Notwithstanding this limitation, the sensitivity and specificity of MRMPI are at least as good as those published for SPECT and stress echocardiography.

QUANTIFICATION

Qualitative visual analysis of MRMPI is adequate in a clinical setting and has been the chosen method of analysis in several studies.¹¹⁻¹⁵⁻¹⁷⁻¹⁹ However, there is a concern that the detection of regions of hypoperfusion is dependent on adjacent areas of myocardium having more (normal) perfusion. In the rarest situation of balanced three-vessel coronary disease, where all segments of myocardium enhance at a similar rate, this might be misinterpreted as normal if visual analysis is used alone. This has led to the development of semi and fully quantitative parameters, which can be measured using data from the first-pass kinetics of gadolinium as it perfuses the myocardium. Signal time-intensity curves of segments of myocardium can be drawn and the data can be smoothed using a mathematical function such as γ variate or linear fit model.²⁰ Using these curves, perfusion defects can be identified as having lower peak

signal intensity, and the time taken for hypoperfused areas of myocardium to reach their peak is longer. The most useful, widely accepted semiquantitative parameter is the upslope of the signal intensity versus time curve. Several studies have used this method of assessment of myocardial perfusion.¹⁰⁻¹²⁻¹³ Other measurable semiquantitative parameters include the mean transit time of the gadolinium through a chosen section of myocardium and the area under the signal intensity curve up to the point it reaches its peak signal intensity. An even more detailed quantification involves calculating the myocardial perfusion reserve by measuring the ratio of the normalised upslopes for segments of myocardium at rest and under conditions of hyperaemia.¹⁴⁻²¹ The absolute quantification of myocardial perfusion reserve is difficult and requires deconvolution of the measured myocardial signal intensity curve with the arterial input function signal intensity curve. This approach can be carried out only at low doses of contrast agent, where there is a linear relationship between changes in signal intensity and contrast concentration within the left ventricle. This method is detailed along with a review of semi and fully quantitative perfusion analysis by Jerosch-Herold *et al.*²⁰

LIMITATIONS

All methods of assessing myocardial perfusion have their limitations and with each technique there are subgroups of patients who cannot be examined. There are also several standard contraindications to magnetic resonance imaging (MRI), including implantable cardioverter defibrillators and other metallic surgical implants, which cannot be inserted into the magnetic field of the scanner. It is safe to scan patients with certain types of pacemaker, but this should be done only when absolutely necessary and in the presence of a trained doctor and cardiac technician with pacemaker programming facilities. There are very few contraindications to the use of gadolinium; however, patients with sickle cell or haemolytic anaemia should be avoided. Severely obese or claustrophobic patients often have poor tolerance of MRI in general. One study has compared the tolerance of MRMPI with that of SPECT in 41 consecutive patients who underwent both examinations. The authors reported that more patients preferred MRI (12 v 9) and concluded that MRMPI was an acceptable alternative in terms of patient tolerance and satisfaction.

Patients with atrial fibrillation or frequent supraventricular or ventricular ectopic beats present a challenge. The scanner triggers on these complexes, leading to the acquisition of the images in different phases of the cardiac cycle, causing artefact and making the images more difficult to interpret. "Dark rim artefact", which is thought to be due to susceptibility within the subendocardium, can be caused by the bright gadolinium bolus within the left ventricular cavity and also by cardiac

Table 1 Magnetic resonance myocardial perfusion imaging studies 2001–5

Author	Year	Patients	Sensitivity	Specificity	Comparison
Schwitzer ¹²	2001	66 (incl 18 volunteers)	91/87	94/85	PET/QCA ($\geq 50\%$)
Ibrahim ¹³	2002	59 (incl 34 volunteers)	69/86	89/84	QCA ($>75\%$)/PET
Nagel ¹⁴	2003	84	88	90	QCA ($\geq 75\%$)
Ishida ¹⁵	2003	104	90	85	QCA ($\geq 70\%$)+SPECT
Plein S ¹⁶	2004	68	88	83	Angiography ($\geq 70\%$)
Paetsch ¹¹	2004	79	91	62	QCA ($>50\%$)
Takase B ¹⁷	2004	102	93	85	Angiography ($>50\%$)
Giang ¹⁰	2004	80	94/91/94*	25/78/71*	QCA ($\geq 50\%$)
Plein ¹⁸	2005	102 (incl 10 volunteers)	88	82	Angiography ($>70\%$)

PET, positron emission tomography; QCA, quantitative coronary angiography; SPECT, single photon emission computed tomography. *Various contrast medium doses (0.05/0.10/0.15 mmol/kg).

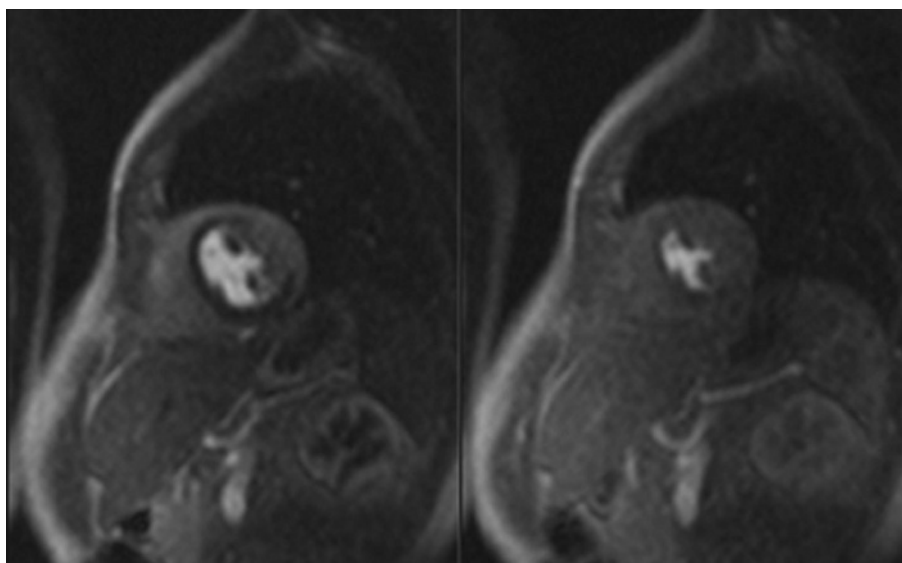


Figure 1 Mid-ventricular adenosine stress MRMPI in a patient while at stress (left) and rest (right) with severe left anterior descending and right coronary artery disease. The dark subendocardial rim indicates the extent of the hypoperfusion.

motion.²² There are also potential problems in trying to obtain adequate coverage of the total left ventricular myocardium (temporal resolution) while maintaining a high spatial resolution for the delineation of sub-endocardial and transmural perfusion defects. Most centres which acquire images during every R–R interval will achieve only three or four slices of myocardium and may conceivably miss a perfusion defect in a remote section of the myocardium.

THE FUTURE

New and faster imaging sequences such as k-t BLAST allow better coverage of the left ventricle while achieving adequate spatial resolution. Potential improvements in SNR and temporal resolution may be achievable at higher magnetic field strengths such as 3 Tesla. However, there are problems with susceptibility artefacts that need to be overcome. New contrast agents such as intravascular T1 enhancing agents are being developed. Commercially available software for correction of cardiac and respiratory motion is available and is improving, although far from perfect. Similarly, although quantification of myocardial perfusion is currently labour intensive and time consuming, less labour-intensive methods are being developed.^{23–24} As these techniques evolve, MRMPI may, in due course, probably replace SPECT as the most widely used non-invasive method for the detection of reversible myocardial ischaemia.

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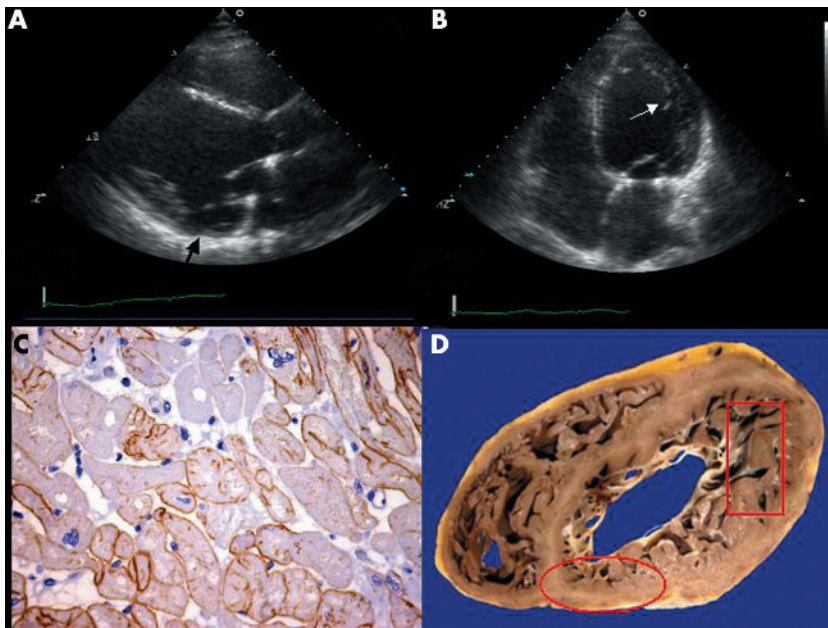
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Echocardiographic clues to diagnosis of dystrophin related dilated cardiomyopathy

A 32-year-old man with a four-year history of congestive heart failure was referred to our institution. Two years previously, the patient had received a diagnosis of idiopathic dilated cardiomyopathy with severe secondary mitral insufficiency. Clinical reappraisal focused attention on the following features: (1) normal coronary arteries at angiography; (2) constantly elevated creatine phosphokinase (CPK) plasma values (300–450 mU/ml); (3) localised inferobasal left ventricular akinesia and thinning (arrow in panel A); (4) spongy appearance of the apicolateral left ventricular wall (arrow in panel B), suggesting ventricular non-compaction. It was also noted that the patient had been complaining of muscular asthenia (hitherto ascribed to heart failure), especially of the lower limbs. Suspected dystrophinopathy was confirmed after myocardial and peripheral muscle biopsies; immunostaining of myocardial tissue (panel C) for detection of N-terminal domain of dystrophin (monoclonal antibody NCL-DYSB, clone 34C5, Novocastra) revealed discontinuous and partially disrupted positive myocytes (of varying intensity) interspersed with negative myocytes. The final diagnosis was dystrophin related, severe dilated cardiomyopathy in a patient with neurologically mild Becker disease. Surgical mitral valve annuloplasty was attempted, but heart failure continued to worsen during the following two years. Heart transplantation was successfully performed. Macroscopic examination of the explanted organ confirmed the localised inferobasal left ventricular thinning (oval in panel D) and the presence of left ventricular non-compaction (rectangle in panel D).

In many cases dilated cardiomyopathy should nowadays no longer be considered a final diagnosis, but rather a starting point for further assessment. Molecular biology techniques increasingly allow identification of distinct aetiologies that share the dilated



cardiomyopathy phenotype. At each diagnostic step, the clinician needs to recognise highly specific (though not sensitive) signs that can be indicative of the true final diagnosis. In the present case, the echocardiogram contains two such “red flags”—namely, ventricular non-compaction and localised inferobasal left ventricular akinesia. Taken separately, either of these signs would raise a strong suspicion of dystrophinopathy. When combined, they are almost pathognomonic.

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